

Label-free monitoring of microcapsule-enabled intracellular release using gold-nanoparticle coated microchips

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By using gold and silver nanostructures for intracellular SERS, several applications of highly sensitive and selective label-free single cell analysis have been demonstrated^[1]. While colloidal nanoparticles have been shown to be minimally invasive to cells, these experiments suffer from a poor reproducibility due to the unpredictable behaviour of the nanoparticles. On the other hand, Tip-Enhanced RS probes contain a fixed metal nanopattern, but intracellular applications with these probes require an incision of the cell membrane during the measurement. In order to enable intracellular SERS detection with a fixed metal pattern, but without an incision of the cell wall during measurements, we fabricated micron-sized silicon-nitride chips using UV contact lithography. These planar structures are entirely incorporated by the cell and offer a high surface/volume ratio, which maximizes the probe area and is expected to limit cytotoxicity. Equally important, our fabrication scheme allows to use the wide variety of

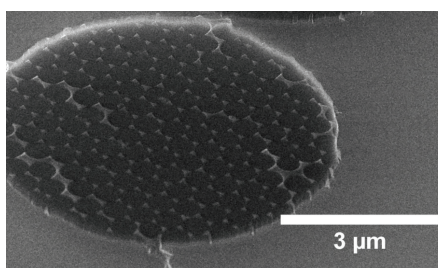
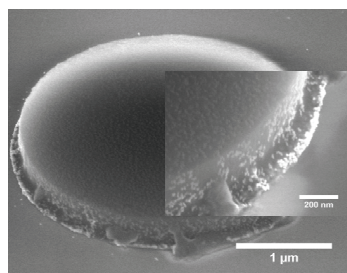


Figure 1: SEM image of a SiN chips coated with adsorbed gold nanoparticles (left) and nanosphere-lithography fabricated gold triangles (right)

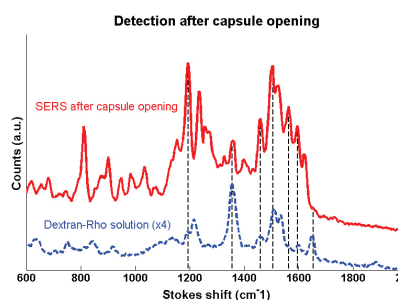
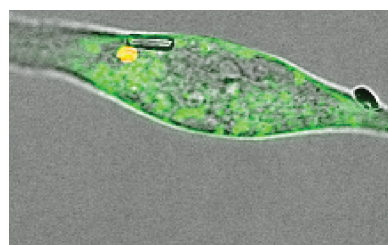


Figure 2: (left) Human fibroblast cell containing dextran-rhodamin loaded capsules (yellow) next to a rectangular gold SiN chip with adsorbed gold nanoparticles (right) SERS spectra measured on top of the SiN chips after capsule release (red) and reference spectrum of dextran-rhodamin

concentration (1mg/ml) of D-RhoB is loaded into a polymeric capsule^[2]. These capsules and the gold-coated SiN chips are delivered into the cytoplasm of a cell via electroporation (fig 2, left). Next, a specific capsule is opened through laser-triggered heating. Immediately afterwards, SERS spectra are collected on top of a SiN chip in the same cell. Despite the complex intracellular environment, specific SERS peaks originating from the released D-RhoB are observed at low laser power (1-2mW) and short integration time (500msec) (fig2, right). This experiment indicates the potential of our approach for monitoring (in-vitro) drug delivery. Furthermore the planar SiN chips enable us to design more complex photonic chips and gold coatings in the near future.

[1] E. Vitol et al., *J Raman Spectrosc.*, 2012, 43-7, 817-27, [2] A. Skirtach et al., *Nano Letters*, 2005, 5-7 1371-77